

Parameters	Variable	Units	Mice	
			Male	Female
Body Weight	BW	kg	0.03	0.03

**SPECIAL FLOW RATES**

Alveolar Ventilation (unscaled)	QPC	L/h/kg <sup>0.75</sup>	29.1	29.1
Unscaled Cardiac Output	QCC	L/h/kg <sup>0.75</sup>	20.1	20.1

\*Model parameters were optimized with ACSL-optimize (version 11.8.4) as stated in Yang et al. 2012 usir

**FRACTIONAL BLOOD FLOWS TO TISSUES**

Flow to Liver as fraction Cardiac Output	QLC	unitless	0.161	0.161
Flow to Fat as fraction Cardiac Output	QFC	unitless	0.07	0.07
Flow to Slow as fraction Cardiac Output	QSC	unitless	0.159	0.159
Flow to Kidney as fraction Cardiac Output	QKC	unitless	0.09	0.09

**FRACTIONAL VOLUMES OF TISSUES**

Volume Liver as fraction Body Weight	VLC	unitless	0.055	0.055
Volume Lung as fraction Body Weight	VLUC	unitless	0.0073	0.0073
Volume Fat as fraction Body Weight	VFC	unitless	0.1	0.1
Volume Rapid Perfused as fraction Body Weight	VRC	unitless	0.08098	0.08098
Volume Slow Perfused as fraction Body Weight	VSC	unitless	0.384	0.384
Volume Kidney as fraction Body Weight	VKC	unitless	0.0167	0.0167

**PARTITION COEFFICIENTS**

Liver/Blood Partition Coefficient	PL	unitless	1.26	1.26
Lung/Blood Partition Coefficient	PLU	unitless	2.38	2.38
Fat/Blood Partition Coefficient	PF	unitless	17.35	17.35
Slow/Blood Partition Coefficient	PS	unitless	0.59	0.59
Rapid/Blood Partition Coefficient	PR	unitless	1.76	1.76
Blood/Air Partition Coefficient	PB	unitless	7.8	7.8
Kidney/Blood Partition Coefficient	PK	unitless	1.76	1.76
<b>Molecular weight</b>	MW	g/mol	88.5	88.5

**KINETIC CONSTANTS  
DOSING INFORMATION**

Initial concentration CONC ppm

## 018 Chloroprene Model Parameters

Source	Rats		Source
	Male	Female	
Brown et al. 1997 (Table 1)	0.25	0.25	Brown et al. 1997 (p.413)
Brown et al. 1997 (Table 1)	22.4	22.4	Brown et al. 1997 (Table 31)
Marino et al. 2006 (QPC/QCC = 1.45)	18.7	18.7	Brown et al. 1997 (Table 22)
 Using Brown et al. 1997 values initially			
Brown et al. 1997 (Table 23)	0.183	0.183	Brown et al. 1997 (Table 23)
Brown et al. 1997 (Table 23; Same as rat value)	0.07	0.07	Brown et al. 1997 (Table 23)
Brown et al. 1997 (Table 23); Same as that reported for muscle	0.278	0.278	Brown et al. 1997 (Table 23); Same as that reported for muscle
Brown et al. 1997 (Table 23)	0.14	0.14	Brown et al. 1997 (Table 23)
	0.0366	0.0366	
Brown et al. 1997 (Table 4)			Brown et al. 1997 (Table 5)
Brown et al. 1997 (Table 4)	0.005	0.005	Brown et al. 1997 (Table 5)
	0.1	0.1	
Brown et al. 1997 (Table 10)			Brown et al. 1997 (Table 13)
Brown et al. 1997 (Table 4); Sum of adrenals, brain, stomach, small intestine, large intestine, heart, lungs, pancreas, spleen and thyroid	0.04644	0.04644	Brown et al. 1997 (Table 5); Sum of adrenals, brain, stomach, small intestine, large intestine, heart, lungs, pancreas, spleen and thyroid
Brown et al. 1997 (Table 4); Same as that reported for muscle	0.4	0.4	Brown et al. 1997 (Table 5); Same as that reported for muscle
Brown et al. 1997 (Table 4)	0.0073	0.0073	Brown et al. 1997 (Table 5)

Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet	1.58	1.58	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet	1.85	1.85	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet	16.99	16.99	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet	0.6	0.6	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet	2.29	2.29	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet	7.3	7.3	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet	2.29	2.29	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
<a href="https://pubchem.ncbi.nlm.nih.gov/compound/31369#section=Chemical-and-Physical-Properties">https://pubchem.ncbi.nlm.nih.gov/compound/31369#section=Chemical-and-Physical-Properties</a>	88.5	88.5	<a href="https://pubchem.ncbi.nlm.nih.gov/compound/31369#section=Chemical-and-Physical-Properties">https://pubchem.ncbi.nlm.nih.gov/compound/31369#section=Chemical-and-Physical-Properties</a>

See Metabolism Parmas Tab in Excel Workbook

<b>Humans</b>	<b>Source</b>
<b>Mixed</b>	
70	Brown et al. 1997 (p.415)
27.75	Clewel et al. 2001 (Table 1)
12.89	Clewel et al. 2001 (Table 1)
0.227	Brown et al. 1997 (Table 23)
0.052	Brown et al. 1997 (Table 23)
0.191	Brown et al. 1997 (Table 23); Same as that reported for muscle
0.175	Brown et al. 1997 (Table 23)
0.0257	
	Brown et al. 1997 (Table 7)
0.0076	Brown et al. 1997 (Table 7)
0.27	Brown et al. 1997 (Table14); Average of total male and female
0.0533	Brown et al. 1997 (Table 7); Sum of adrenals, brain, stomach, small intestine, large intestine, heart, lungs, pancreas, spleen and thyroid
0.4	Brown et al. 1997 (Table 7); Same as that reported for muscle
0.0044	Brown et al. 1997 (Table 7)

2.37	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
2.94	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
28.65	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
1.00	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
2.67	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet
4.5	Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet

2.67 Yang et al. 2012 (Table 2); Calculated using tissue:air PC reported in Himmelstein et al. (2004);See Partition Conversion sheet  
<https://pubchem.ncbi.nlm.nih.gov/compound/31369#section=Chemical-and-Physical-Properties>



# METABOLIC PARAMETERS AND SCALING/CONVERSION

## MICE & RAT&HUMAN Conversion of Metabolic Parameters obtained from original ACSLX code for PBPK model

$$VMAXC = VMAXC10(SPECIES) * LiverCovVmax(SPECIES) * VLC * BW^{0.25}$$

$$VMAXCLU = VMAXCLU10(SPECIES) * LungCovVmax(SPECIES) * VLUC * BW^{0.25}$$

$$VMAXCKID = VMAXCKID0(SPECIES) * KidCovVmax(SPECIES) * VKC * BW^{0.25}$$

$$KM = KM10(SPECIES) * LiverCovKm(SPECIES)$$

$$KMLU = KMLU10(SPECIES) * LungCovKm(SPECIES)$$

$$KMKD = KMKD0(SPECIES) * KidCovKm(SPECIES)$$

$$KFLUC = KFLU0(SPECIES) * LungCovVK(SPECIES) * VLUC$$

	VmaxC10	KM10	MICE & RAT&HUMAN Conv	
			VmaxCLU10	KMLU10
Female Mouse	0.09	0.53	0.025	2.78
Male Mouse	0.26	1.36	0.13	2
Female Rat	0.068	0.82	0	1
Male Rat	0.077	0.56	0	1
Human	0.054	0.45	0	1

## SCALED METABOLIC VALUES USED IN MODELING

Sex & Species	Parameters	Scaled Yang et al. 2012 Table 3 Values (rscript 3)	Reported Yang et al. 2012 Table 2 Values (rscript 2)
Female Mouse	Vmaxc (mg/h/BW <sup>0.75</sup> )	6.3863	8.88
	VmaxcLU (mg/h/BW <sup>0.75</sup> )	0.1486	0.11
	VmaxcKID (mg/h/BW <sup>0.75</sup> )	0.0003	0.03
	KM (mg/L)	0.0469	0.08
	KMLU (mg/L)	0.2460	0.25
	KMKD (mg/L)	0.1505	9.59
	KFLUC (L/h/BW <sup>0.75</sup> )	0	0
Male Mouse	Vmaxc (mg/h/BW <sup>0.75</sup> )	18.4492	18.54
	VmaxcLU (mg/h/BW <sup>0.75</sup> )	0.7726	0.6
	VmaxcKID (mg/h/BW <sup>0.75</sup> )	0.0716	0.078
	KM (mg/L)	0.1204	0.12
	KMLU (mg/L)	0.1770	0.2
	KMKD (mg/L)	0.0443	0.068
	KFLUC (L/h/BW <sup>0.75</sup> )	0	0
	Vmaxc (mg/h/BW <sup>0.75</sup> )	7.0647	9.37

Female Rat	VmaxcLU (mg/h/BW <sup>0.75</sup> )	<b>0</b>	<b>0</b>
	VmaxcKID (mg/h/BW <sup>0.75</sup> )	<b>0.0087</b>	<b>0.018</b>
	KM (mg/L)	<b>0.0726</b>	<b>0.09</b>
	KMLU (mg/L)	<b>0.0885</b>	<b>0.25</b>
	KMKD (mg/L)	<b>0.0327</b>	<b>0.053</b>
	KFLUC (L/h/BW <sup>0.75</sup> )	<b>0.1380</b>	<b>0.16</b>
Male Rat	Vmaxc (mg/h/BW <sup>0.75</sup> )	<b>7.9997</b>	<b>9.48</b>
	VmaxcLU (mg/h/BW <sup>0.75</sup> )	<b>0</b>	<b>0</b>
	VmaxcKID (mg/h/BW <sup>0.75</sup> )	<b>0.0133</b>	<b>0.018</b>
	KM (mg/L)	<b>0.0496</b>	<b>0.05</b>
	KMLU (mg/L)	<b>0.0885</b>	<b>0.25</b>
	KMKD (mg/L)	<b>0.0814</b>	<b>0.067</b>
Human	Vmaxc (mg/h/BW <sup>0.75</sup> )	<b>20.2317</b>	<b>20.4</b>
	VmaxcLU (mg/h/BW <sup>0.75</sup> )	<b>0</b>	<b>0</b>
	VmaxcKID (mg/h/BW <sup>0.75</sup> )	<b>0</b>	<b>0</b>
	KM (mg/L)	<b>0.0398</b>	<b>0.04</b>
	KMLU (mg/L)	<b>0.0885</b>	<b>0.25</b>
	KMKD (mg/L)	<b>0.0885</b>	<b>9.59</b>
	KFLUC (L/h/BW)	<b>0.1656</b>	<b>0.05</b>

# EXTRACTION AND METABOLISM CALCULATIONS FOR CHLOROPRENE PE

## Reference

From ACSLX  
GeneralMice.m;  
GeneralRat.m;  
GeneralHuman.m

## Extraction Constants Used for Equation/In Vitro metabolism values from Yang et al

VmaxCKID0	KMKID10	KFLU0	LiverCovVmax
0.00004	1.7	0	3100
0.01	0.5	0	3100
0.00177	0.37	0.0012	4340
0.0027	0.92	0.0009	4340
0	1	0.0009	5040

Optimization of Scaled  
Fixed KM (Optimization  
Spreadsheet)  
(rscript5)

8.5150      8.5150

0.0594

0.0007

0.0841

0.0841

0.0841

0

14.9013

0.2972

0.0716

0.0841

0.0841

0.0841

0

5.7141

	0.0044
	0.0133
	0.0611
	0.0611
	0.0611
	0
	<b>8.9347</b>
	0.0045
	0.0111
	0.0611
	0.0611
	0.0611
	0
	<b>20.2317</b>
	0.0191
	0
	0.0398
	0.0398
	0
	0

## 3PK MODEL

I. (2012) Table 3 (Data for Calculations obtained from ACSLX PBPK model Parameters.m file)

LiverCovKm	LungCovVmax	LungCovKm	KidCovVmax	KidCovKm
0.0885	2040	0.0885	1030	0.0885
0.0885	2040	0.0885	1030	0.0885
0.0885	2040	0.0885	1030	0.0885
0.0885	2040	0.0885	1030	0.0885
0.0885	2040	0.0885	1030	0.0885

Optimization of  
Fixed KM Values  
Used for Scaled  
Metabolic  
Parameters

0.12  
0.01  
0.00009962  
0.95  
0.95  
0.95  
0

0.21  
0.05  
0.01  
0.95  
0.95  
0.95  
0

0.055

1.02
0.0027
0.69
0.69
0.69
0
0.086
1.86
0.002264
0.69
0.69
0.69
0
0.054
0.405
0
0.45
0.45
0
0

LungCovVK	VLC	VLUC	VKC	BW
23000	0.055	0.007	0.0167	0.03
23000	0.055	0.007	0.0167	0.03
23000	0.0366	0.005	0.0073	0.183
23000	0.0366	0.005	0.0073	0.183
23000	0.0257	0.008	0.0044	70

# Documentation and Description

## Title of Model File (bottom right pane of R Studio)

chloroprene.model

chloroprene.model\_inits.R

Chloroprene\_fin.Rproj

Female\_mouse\_dose\_metric\_2

Female\_mouse\_dose\_metric\_3

Female\_mouse\_dose\_metric\_5

Female\_mouse\_invivo\_3.R

Female\_mouse\_invivo\_5.R

Female\_rat\_dose\_metric\_2.R

Female\_rat\_dose\_metric\_3.R

Female\_rat\_dose\_metric\_5.R  
firstbuildmodel.R

forfunc.R

Human\_dose\_metric\_1ppbcont.R

Human\_dose\_metric\_1ppmcont.R

Human\_dose\_metric\_2.R

Human\_dose\_metric\_3.R

Human\_dose\_metric\_5.R

Male\_mouse\_dose\_metric\_2.R

Male\_mouse\_dose\_metric\_3.R

Male\_mouse\_dose\_metric\_5.R

Male\_rat\_dose\_metric\_2.R

Male\_rat\_dose\_metric\_3.R

Male\_rat\_dose\_metric\_5.R

mouse13.csv

mouse32.csv

mouse90.csv

```
params  
rebuildmodel.R  
states.R
```

# Description of Script files in Chloroprene PBPK Model

## Description

This script is the Chloroprene PBPK Model and contains its code.

This script sets the initial input, output and state variables that are used in the model.

This is the PBPK model project workspace that contains the model and script files associated with the model.

Script file simulates the female mouse following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using metabolic constants reported in Yang et al. 2012 Table 2. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the female mouse following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using the scaled metabolic data reported in Yang et al. 2012 Table 3. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the female mouse following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using the scaled metabolic data reported for fixed Km optimized values. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

R script simulates the 15 day mouse nose-only inhalation exposure study of chloroprene (12.3, 30.0, 90.0 ppm) with data collected during and after exposure on the 1st day and at the end of exposure on day 5 and 15. This script uses the scaled metabolic parameters from Yang et al. 2013 and outputs 3 graphs that plot model estimated lung tissue concentrations (CVLUM) against time and data sets for day 1, 5 and 19.

R script simulates the 15 day mouse nose-only inhalation exposure study of chloroprene (12.3, 30.0, 90.0 ppm) with data collected during and after exposure on the 1st day and at the end of exposure on day 5 and 15. This script uses the scaled metabolic data reported for fixed Km optimized values and outputs 3 graphs that plot model estimated lung tissue concentrations (CVLUM) against time and data sets for day 1, 5 and 19.

Script file simulates the female rat following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using metabolic constants reported in Yang et al. 2012 Table 2. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the female rat following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using the scaled metabolic data reported in Yang et al. 2012 Table 3. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the female rat following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using the scaled metabolic data reported for fixed Km optimized values. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file that will initially build the model to begin scenario simulations.

Script file that contains the exposure commands such as the length of exposure in hours, how many days per week exposed and the number of days of animal exposure.

R script file simulates human continuous exposure to 1 ppb of chloroprene for 2 weeks using metabolism parameters reported in Yang et al. 2012 Table 2, Yang et al. 2012 Table 3 and scaled metabolic data reported for fixed Km optimized values. This script outputs a table that contains the exposure concentration and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

R script file simulates human continuous exposure to 1 ppm of chloroprene for 2 weeks using metabolism parameters reported in Yang et al. 2012 Table 2, Yang et al. 2012 Table 3 and scaled metabolic data reported for fixed Km optimized values. This script outputs a table that contains the exposure concentration and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the human following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using metabolic constants reported in Yang et al. 2012 Table 2. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the human following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using the scaled metabolic data reported in Yang et al. 2012 Table 3. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).  
Script file simulates the human following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using the scaled metabolic data reported for fixed Km optimized values. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the male mouse following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using metabolic constants reported in Yang et al. 2012 Table 2. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the male mouse following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using the scaled metabolic data reported in Yang et al. 2012 Table 3. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the male mouse following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using the scaled metabolic data reported for fixed Km optimized values. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the male rat following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using metabolic constants reported in Yang et al. 2012 Table 2. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the male rat following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using the scaled metabolic data reported in Yang et al. 2012 Table 3. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Script file simulates the male rat following 2 weeks of exposure 6 hours/day, 5 days/week, of chloroprene (12.3, 32.0, 80.0 ppm) using the scaled metabolic data reported for fixed Km optimized values. This script outputs a table that contains the exposure concentrations and the estimated concentrations in the liver (AMP), lung (AMPLU) and kidney (AMPK).

Data files for the plot for female mouse *in vivo* nose-only 15 day study (12.3 ppm)

Data files for the plot for female mouse *in vivo* nose-only 15 day study (32 ppm)

Data files for the plot for female mouse *in vivo* nose-only 15 day study (90 ppm)

Folder that contains all physiological parameters called in by R-script scenario files and includes:

Female\_Mouse\_2.R - Uses metabolic parameters from Yang et al. 2012 Table 2

Female\_Mouse\_3.R - Uses scaled metabolic parameters from Yang et al. 2012 Table 3

Female\_Mouse\_5.R - Uses scaled metabolic parameters from reoptimized fixed Km values

Female\_Rat\_2.R - Uses metabolic parameters from Yang et al. 2012 Table 2

Female\_Rat\_3.R - Uses scaled metabolic parameters from Yang et al. 2012 Table 3

Female\_Rat\_5.R - Uses scaled metabolic parameters from reoptimized fixed Km values

Human\_2.R - Uses metabolic parameters from Yang et al. 2012 Table 2

Human\_3.R - Uses scaled metabolic parameters from Yang et al. 2012 Table 3

Human\_5.R - Uses scaled metabolic parameters from reoptimized fixed Km values

Male\_Mouse\_2.R - Uses metabolic parameters from Yang et al. 2012 Table 2

Male\_Mouse\_3.R - Uses scaled metabolic parameters from Yang et al. 2012 Table 3

Male\_Mouse\_5.R - Uses scaled metabolic parameters from reoptimized fixed Km values

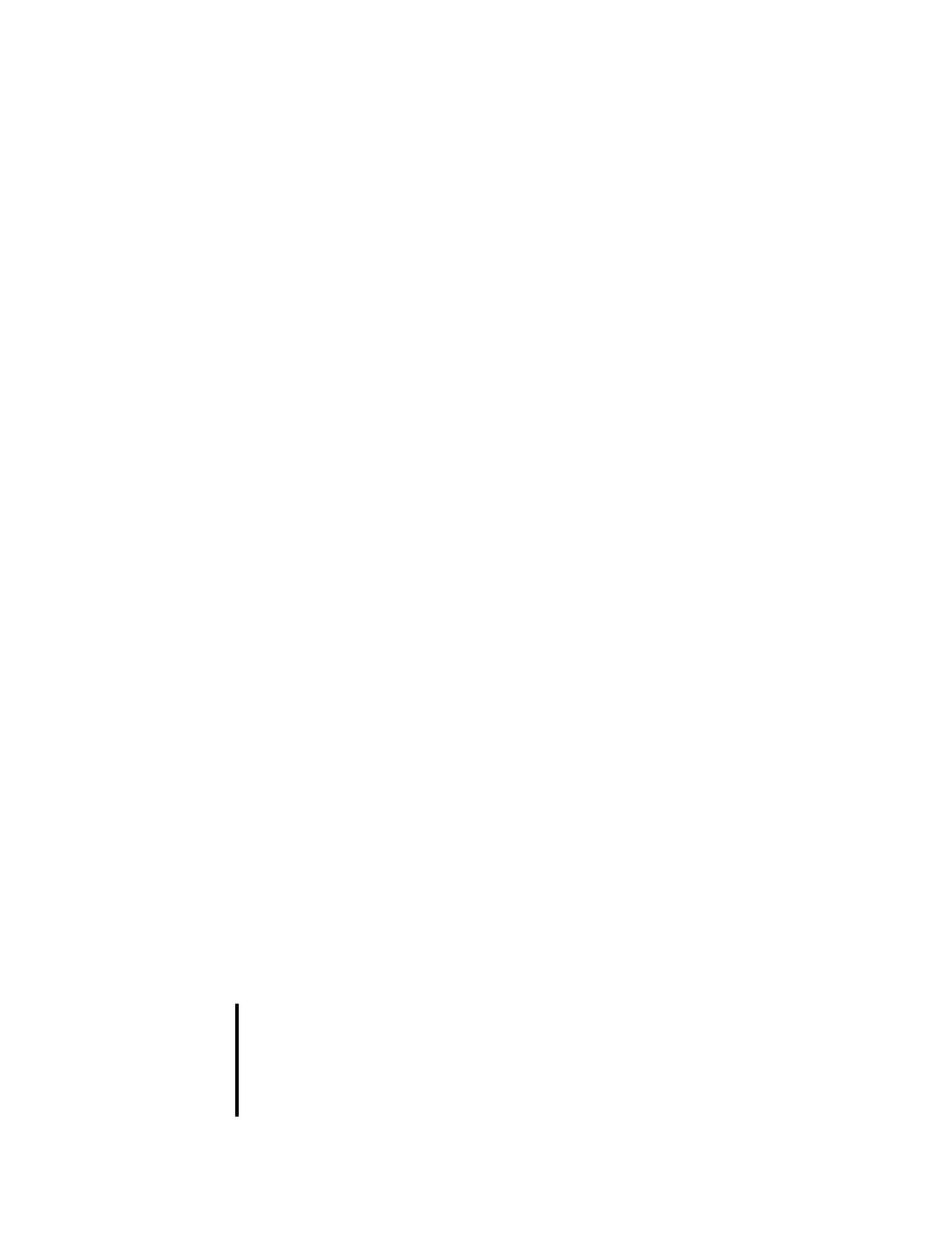
Male\_Rat\_2.R - Uses metabolic parameters from Yang et al. 2012 Table 2

Male\_Rat\_3.R - Uses scaled metabolic parameters from Yang et al. 2012 Table 3

Male\_Rat\_5.R - Uses scaled metabolic parameters from reoptimized fixed Km values

R script to re-build the model code if needed after run of initial build.

R script which defines initial state values.



JLC ran after revising the error tolerance for the integration algorithm

TSTOP

Exposure:

**Yang et al. 2012 Table 2 Metabolic**

ppm	Female Mouse InitialParms		
	AMP	AMPLU	AMPK
12.3	1.488	0.702	0.0033
32	3.910	1.161	0.0084
80	9.739	1.552	0.0204

**Yang et al. 2012 Table 3 Estimated N**

ppm	Female Mouse Initial Parm	
	AMP	AMPLU
12.3	1.474	0.948
32	3.888	1.571
80	9.582	2.107

ppm	Male Mouse InitialParms		
	AMP	AMPLU	AMPK
12.3	1.197	3.794	0.341
32	3.447	6.484	0.478
80	9.295	8.620	0.558

ppm	Male Mouse InitialParms	
	AMP	AMPLU
12.3	1.101	5.001
32	3.286	8.565
80	9.093	11.280

ppm	Female Rat InitialParms		
	AMP	AMPLU	AMPK
12.3	0.436	0.113	0.074
32	1.142	0.298	0.095
80	2.856	0.751	0.113

ppm	Female Rat InitialParms	
	AMP	AMPLU
12.3	0.440	0.099
32	1.149	0.259
80	2.855	0.655

ppm	Male Rat InitialParms		
	AMP	AMPLU	AMPK
12.3	0.896	0.215	0.135
32	2.348	0.564	0.181
80	5.880	1.421	0.218

ppm	Male Rat InitialParms	
	AMP	AMPLU
12.3	0.906	0.150
32	2.365	0.394
80	5.904	0.991

ppm	Human InitialParms		
	AMP	AMPLU	AMPK
12.3	0.253	0.040	0
32	0.658	0.105	0
80	1.645	0.263	0

ppm	Human InitialParms	
	AMP	AMPLU
12.3	0.240	0.127
32	0.625	0.331
80	1.562	0.827

Continuous Exposure

ppm	Human Parms extended cor	
	AMP	AMPLU
0.0016	0.0001741	9.2061E-05
0.016	0.0017405	0.00092061
10	1.0878	0.5754
50	5.4374	2.8773
100	10.8708	5.7555
300	32.5317	17.2844
600	63.6504	34.8843

	<b>Human Continuous Exposure</b>	
	<b>Human Params Continuous</b>	
	PPM	AMU
Yang et al. 2012	Table 2	1 0.115
Yang et al. 2012	Table 3	1 0.109
Fixed Km	Revised	1 0.109

	<b>Human Continuous Exposure</b>	
	<b>Human Params Continuous</b>	
	PPM	AMU
Yang et al. 2012	Table 2	0.001 1.15E-04
Yang et al. 2012	Table 3	0.001 1.09E-04
Fixed Km	Revised	0.001 1.09E-04

**168 hrs**  
**6 hr/day 5 days/week**

**Metabolic**

AMPK	0.001063
	0.001578
	0.001958

**Fixed Km**

**Female Mouse InitialParms**

ppm	AMP	AMPLU	AMPK
12.3	1.488	0.657	0.003243
32	3.924	0.866	0.004276
80	9.730	1.004	0.004958

**Male Mouse InitialParms**

ppm	AMP	AMPLU	AMPK
12.3	1.267	3.036	0.290
32	3.643	4.193	0.416
80	9.606	4.911	0.491

**Female Rat InitialParms**

ppm	AMP	AMPLU	AMPK
12.3	0.445	0.031	0.047
32	1.163	0.041	0.062
80	2.882	0.049	0.074

**Male Rat InitialParms**

ppm	AMP	AMPLU	AMPK
12.3	0.914	0.048	0.080
32	2.392	0.062	0.105
80	5.978	0.074	0.125

**Human InitialParms**

ppm	AMP	AMPLU	AMPK
12.3	0.253	0.039	0
32	0.666	0.055	0
80	1.672	0.078	0

**Continuous Exposure**

**Human Parms extended conc.**

ppm	AMP	AMPLU	AMPK
0.0016	0.000174	9.22E-05	0
0.016	0.001741	0.000919	0
10	1.15	0.1636	0
50	5.83	0.2087	0
100	11.68	0.2160	0
300	35.01	0.2212	0
600	67.46	0.2225	0

**sure (1 ppm)**

s Exposure	
AMPLU	AMPK
0.0183	0
0.0575	0
0.0464	0

**sure (1 ppb)**

s Exposure	
AMPLU	AMPK
1.83E-05	0
5.75E-05	0
5.76E-05	0